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EXAMINER	
ZEMAN, ROBERT A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/657,126	BOUQUET ET AL.	
	Examiner	Art Unit	
	ROBERT A. ZEMAN	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-14,16-19 and 27-37* is/are pending in the application.

4a) Of the above claim(s) *1-6,8-10,14 and 27-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-13, 16-19 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 4-7-2009 are acknowledged. Claims 35 and 37 have been amended. Claims 1-6, 8-14, 16-19 and 27-37 are pending. Claims 1-6, 8-10, 14, and 27-33 remain withdrawn from consideration. Claims 11-13, 16-19 and 34-37 are currently under examination.

Claim Rejections Withdrawn

The rejection of claims 35 and 37 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (deposit requirement) is withdrawn in light of the declaration filed on 4-7-2009

The rejection of claims 35 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "derived from the cell line TDF-2A bcl-2" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

The provisional rejection of claims 12 and 14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim11, 15-17 and 19 of copending Application No. 11/031,417 is maintained for reasons of record. Applicants have declined to act on this rejection until it is determined whether the claims in the copending application are allowable.

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to an avian cell line which are immortalized, but untransformed, comprising in their genome the SV40 T+t gene. Said cell lines can be obtained from avian tissue.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Written Description

The rejection of claims 11-13, 16-19 and 34-37 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues:

1. The specification discloses a structure-function relationship in the claimed avian cells as the claims recite the genome of the cells comprises a nucleic acid encoding SV40T+t and the cell contains a nucleic acid molecule encoding an antiapoptotic protein.

2. The relationship between structure (SV40 T+t gene) and function (immortalized and untransformed phenotype) set forth in the specification.

3. Even if immortalization of avian cells were difficult to achieve and would dissuade the skilled artisan from trying the present invention, the specification demonstrated how it can be achieved using SV40 T+t.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 2, contrary to Applicant's assertion, the specification does not provide a correlation between structure and function. Example I illustrates the use of a specific vector, pphMT, in which out of all of the clones and subclones transfected with said vector only a single immortalized and untransformed cell line (TCF-4.10) was obtained. If Applicant's assertion was accurate most if not all avian cells transfected with the pphMT vector would exhibit the claimed phenotype. The rarity of the claimed phenotype as exhibited by Example I, supports the declaration by Michel Riviere, who states that not only are avian cells very difficult to immortalize, the use of SV40T+t leads to the transformation in cells (see page 3 of declaration). Consequently, aside from the aforementioned cell lines there exists no correlation between the structure (i.e. genome) and the claimed function (an immortalized and untransformed phenotype) as required for proper written description. Moreover, the nucleic acid encoding the antiapoptotic gene was introduced after the isolation of the aforementioned cells.

With regard to Point 3, the claims are not limited to immortalized cells. The instant claims require that the cells be immortalized but not transformed. As avowed to by Applicant's declarant by Michel Riviere, the use of SV40T+t leads to the transformation in cells (see page 3 of declaration). Moreover, Applicant is reminded that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

As outlined previously, the specification discloses the immortalized but untransformed avian cell lines TDF-2A and TCF-4.10. The specification further discloses the cell lines TDF-2A bcl-2 and TCF--4.10 bcl-2 which are derived from the parent cell lines TDF-2A and TCF-4.10, respectively. These cell lines meet the written description provision of 35 USC 112, *first* paragraph. However, the aforementioned claims are directed to encompass any untransformed, immortalized avian cell comprising a nucleic acid encoding SV40T+t and an antiapoptotic protein. None of these cell lines meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the cell lines TDF-2A, TDF-2A bcl-2, TCF-4.10 and TCF-4.10 bcl-2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Moreover, as forth in the declaration by Michel Riviere, not only are avian cells very difficult to immortalize, the use of SV40T+t leads to the transformation in cells (see page 3 of declaration). Consequently, aside from the aforementioned cell lines there exists no correlation between the structure (i.e. genome) and the claimed function (an immortalized and untransformed phenotype) as required for proper written description. Moreover, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were

found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

> Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli ,* 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood,* 107 F.3d at 1572, 41 USPQ2datl966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only the cell lines TDF-2A, TCF-4.10, TDF-2A bcl-2, and TCF-4.10 bcl-2, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Enablement

The rejection of claims 11-13, 16-19, 34 and 36 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the immortalized and untransformed avian cell lines TDF-2A bcl-2, and TCF-4.10 bcl-2 and the TDF-2A, TCF-4.10 cells that have been transfected with antiapoptotic genes, does not reasonably provide enablement for any other immortalized and untransformed avian cells comprising in its genome a nucleic acid encoding SV40T+t and a nucleic acid encoding an antiapoptotic protein (which is expressed by said cell) is maintained for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant argues:

1. The specification provides ample guidance and direction for the claimed cells. In particular, Example 1 and 3 demonstrates the production of the claimed avian cells and tests to ascertain that the resulting cells are immortalized and absent of tumorigenic capacity.

2. Despite the difficulties in such cells the skilled artisan would not require undue experimentation to arrive at the claimed invention.

Applicant's arguments have been fully considered and deemed unpersuasive.

With regard to Points 1 and 2, contrary to Applicant's assertion, the specification does not provide ample guidance and direction for the claimed invention. Example I illustrates the use of a specific vector, pDAMT, in which out of all of the clones and subclones transfected with said vector only a single immortalized and untransformed cell line (TDF-2A) was obtained. The

same is true for the use of the vector pphMT in Example 3, If Applicant's assertion was accurate most if not all avian cells transfected with said vector would exhibit the claimed phenotype. The rarity of the claimed phenotype as exemplified by Example I, would suggest to the skilled artisan that said phenotype was the result of event other than the mere expression of the SV40T+t antigen. This is supported by the declaration by Michel Riviere that states that not only are avian cells very difficult to immortalize, the use of SV40T+t leads to the transformation in cells (see page 3 of declaration). Consequently, the skilled artisan would not be able to produce an avian cell with the claimed genotypic and phenotypic characteristics without undue experimentation.

As outlined previously, enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be

considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled.

The instant claims are drawn immortalized and untransformed avian cells comprising in its genome a nucleic acid encoding SV40T+t and a nucleic acid encoding an antiapoptotic protein (which is expressed by said cell). However, as disclosed in the declaration by Michel Riviere, not only are avian cells very difficult to immortalize, the use of SV40T+t leads to the transformation in cells (see page 3 of declaration). Consequently, the skilled artisan would not be able to produce an avian cell with the claimed genotypic and phenotypic characteristics without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Claim 37 is rendered vague and indefinite by the use of the phrase "derived from the cell line TCF-4.10 bcl-2". The amendment to said claim is insufficient to overcome this rejection. It is still unclear what is meant by said term as said cell line contains all the features of the claimed cells. It is unclear what constitutes a "derivation" or what features are meant to be encompassed by said derivation. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

New Grounds of Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 35 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Claim 35 is rendered vague and indefinite by the use of the phrase "progeny of the cell line TDF-2A bcl-2. It is still unclear what is meant by said term. Are the “progeny” identical to the recited cell line? If not, what are the features of the claimed “progeny"? Given, that the cell line TDF-2A bcl2 is a progeny cell of TDF-2A into which a heterologous nucleic acid has been introduced, it is impossible to determine what features the claimed progeny cells possess. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Claim 37 is rendered vague and indefinite by the use of the phrase "progeny of the cell line TCF-4.10…”. It is still unclear what is meant by said term. Are the “progeny” identical to the recited cell line? If not, what are the features of the claimed “progeny"? Given, that the cell line TCF-4.10 bcl2 is a progeny cell of TCF-4.10 into which a heterologous nucleic acid has been introduced, it is impossible to determine what features the claimed progeny cells possess. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m. .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Robert A. Zeman/
Primary Examiner, Art Unit 1645
July 6, 2009